Atty. Docket: 000152

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:

Zenoviy TKACHUK

Serial Number: 09/534,509

Group Art Unit: 1633

Filed: March 24, 2000

Examiner: Chen, L.

For: COMPOUND, COMPOSITION AND METHOD FOR THE TREATMENT OF INFLAMMATORY AND INFLAMMATORY-RELATED DISORDERS

DECLARATION UNDER 37 CFR 1.132

Commissioner for Patents
Washington, D.C. 20231

Sir:

I, Vyacheslav PEREDERIY, a citizen of UKRAINE, hereby declare and state:

1. I have a degree of Doctor of Medical Sciences which was conferred upon me by Central Institute of Gastroenterology, in Moscow, Russia, in 1984.

2. I have been employed by the head of sub-faculty of the internal disease of National Medical University in Kyiv, Ukraine, since 1986, and I have accumulated a total of 36 years of work and research experience in the field of medical use of biologically active substances and, specifically, those based on nucleic acids.

3. I am a Board Member of the World Gastrology Association (Organisation Mondiale de Gastro-Enterologie) based at Medconnect, Bruennstrasse 10, 81541 Munich, Germany.

4. My publications include 250 scientific papers and 23 monographs, including the following works:
Immunocorrecting nucleic substances and their clinical use, Kyiv, 1994, 232 pg.,
Interaction of food and medicinal substances, Kyiv, 1992, 240 pg.,
Popular Immunology, Kyiv, 1990, 210 pg.,
Clinical lectures on internal diseases, 2 volumes, Kyiv, 1998, v.1 496 pg., v.2 446 pg.,
Immune status, its principles and correction methods for immune dysfunction, Kyiv, 1995, 210 pg.,

5. My public appearances include speaking at the 9th United European Gastroenterology Week, 6-10 October 2001, in Amsterdam, The Netherlands, on the following subject: Antibiotic resistance of Helicobacter pylori among patient with duodenal peptic ulcer in Ukraine.

6. I have read and understood Dr. Tkachuk's U.S. patent application No. 09/534,509.

7. As a scientist in the field of medicine, I am familiar with the type of experiments reported in Dr. Tkachuk's application. I confirm that such experiments are well know in the art of medical research as reliable predictive tests to establish the efficacy of a compound or composition to treat inflammation.

8. In particular, the experiments reported under the headings Example 4 (carrageenan-induced swelling in rats) and Example 6 (adjuvant arthritis) are conventional experiments from which researchers in the field are able to conclude whether the tested compound or a composition is effective to treat inflammation.

9. The carrageenan test used by Dr. Tkachuk (Example 4 of his patent application) includes all the mechanisms that define the development of an inflammatory process. In this model, basic stages of an inflammatory process include: participation of histamines and serotonins in the first 30 minutes of inflammatory pathogenesis; kinins in the interval between 1.5 and 2.5 hours; prostaglandins in the interval between 2.5-5.5 hours. This test is known as a classical test in pharmacology, which is used along with other tests for screening of anti-inflammatory therapeutical substances, as mentioned by Dr. Thompson in his book Drugs Bioscreening, VCH Publishers, 1990, a very popular publication among pharmacologists.

10. The carrageenan test is cited in many patents dedicated to non-steroid anti-inflammatory drugs. In particular, the carrageenan test, which was employed in vivo by Dr.Tkachuk in Example 4.1, is commonly used for screening of non-steroid drugs for treatment of inflammations, even without evidence obtained from in vivo models, as one can see from US Patent 6,274,177 Wu,et al., August 14,2001.

11. I also confirm that Dr. Tkachuk's methodology for the carrageenan test, as reported in his application, conformed to the conventional procedures for the above experiments. For example, Robert A. Turner in the second paragraph from bottom on page 163 of his popular monograph Screening methods in Pharmacology, Academic Press, NY-London, 1965, pp. 152-163, recommends the carrageenan test for screening of anti-inflammatory drugs.

12. In the conventional carrageenan test, the compound or composition to be tested is administered before the carrageenan injection in accordance with established standards, as was done by Dr. Tkachuk. In pharmacology, there is no separation for preventive and therapeutic substances. Hence, there are no distinct tests applicable to study the two types of drugs. Since inflammatory pathogenesis consists of a chain of mechanisms that follow each other, drugs that influence these processes have both therapeutic and preventive effect. In other words, there are no known non-steroid compounds in pharmacology that have preventive action and do not have a therapeutic effect.

13. Thus, in accordance with the methodology developed by Winder C.A. et al., Proc. Soc. for Exper. Biol. and Med., 1962, III, 544-547, the screened substance shall be injected in animal before the beginning of induction of inflammatory process by carrageenan, in order to monitor the action of such substance in the process of development of the mechanisms of inflammatory pathogenesis. Di Rosa M., Giroud J.P., Willughby D.A., Studies on the mediators of the acute inflammation response induced in rat in different sites by carrageenan and turpentine, J. Patol., V.104,15, p.29 (1971).

14. The experimental results obtained by Dr. Tkachuk regarding the influence of total yeast RNA on the synthesis of prostaglandins at one of the final stages of inflammatory pathogenesis, as reported in Example 4 of his patent application, provide a definite indication of the therapeutic action of the compound in the process of development of the inflammatory disease, rather than of preventive action only.

15. Regarding the adjuvant arthritis model used by Dr. Tkachuk (Example 6 in his patent application), the compound was injected not only before the condition was initiated, but also in the process of development of inflammation, as indicated in Example 6.1, which conforms to the conventional methodology. In this test, analysis of the influence of the compound on NO-synthetase activity shows whether the compound tested is effective, not only at the initial development stages of condition, but also at the final development stages of condition, in its chronic phase.

16. In summary, based on study, in my professional capacity, of the evidence obtained in the several pharmacology-acknowledged tests for studying anti-inflammatory drugs in vitro and in vivo employed in Dr. Tkachuk's work, I have no doubt that total yeast RNA has a therapeutic effect for treatment of inflammations and inflammatory-related conditions in mammals.

The undersigned declares that all statements made herein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code and that willful false statements may jeopardize the validity of the application or any patent issued thereon.

Signed this 21 day of 03, 2002

Signature: _____

Vyacheslav PEREDERIY